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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/060,066	01/29/2002	Alejandro Abuin	LEX-0304-USA	8417

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EXAMINER	
BERTOGLIO, VALARIE E	
ART UNIT	PAPER NUMBER
1632	

DATE MAILED: 11/03/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/060,066	ABUIN ET AL.	
	Examiner	Art Unit	
	Valarie Bertoglio	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *05 May 2005 and 15 August 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1 and 3-7* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1 and 3-7* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *01/29/2002* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submissions filed on 05/05/05 and 08/15/05 have been entered.

Claims 2 and 8 have been cancelled. Claims 1 and 7 have been amended. Claims 1 and 3-7 are pending and under consideration in the instant office action.

Compliance under 37 CFR 1.121

It is noted that cancelled claim 8 is not included in the listing of the claims. The listing of the claims should be a complete listing of all claims ever presented [see 37 CFR 1.121(c)]. In the interest of furthering prosecution, because claim 8 is cancelled, claims 1 and 3-7 are considered on the merits in the instant office action. However, future claim submissions should include all claims, including cancelled claims. The text of cancelled claims should not be included [see 37 CFR 1.121(c)(4)].

Claim Objections

Claims 1 and 7 are objected to because of the following informalities:

Claims 1 and 7 are awkward because of the use of the term "locus". A locus is generally accepted in the art to refer to a particular "address" on a chromosome and not to a gene or allele encoded there. Thus, a locus does not encode exon sequence as claimed. A locus is a location, not a gene. Appropriate correction is required.

Claim 7 is objected to because it does not end in a period. Appropriate correction is required.

Claim Rejections - 35 USC § 101/ 112

35 U.S.C. 101 reads as follows:

Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Definitions:
[from REVISED INTERIM UTILITY GUIDELINES TRAINING MATERIALS; repeated from http://www.uspto.gov/web/menu/utility.pdf]

"Specific Utility" - A utility that is *specific* to the subject matter claimed. This contrasts with a *general* utility that would be applicable to the broad class of the invention. For example, a claim to a polynucleotide whose use is disclosed simply as a "gene probe" or "chromosome marker" would not be considered to be *specific* in the absence of a disclosure of a specific DNA target. Similarly, a general statement of diagnostic utility, such as diagnosing an unspecified disease, would ordinarily be insufficient absent a disclosure of what condition can be diagnosed.

"Substantial utility" - a utility that defines a "real world" use. Utilities that require or constitute carrying out further research to identify or reasonably confirm a "real world" context of use are not substantial utilities. For example, both a therapeutic method of treating a known or newly discovered disease and an assay method for identifying compounds that themselves have a "substantial utility" define a "real world" context of use. An assay that measures the presence of a material which has a stated correlation to a predisposition to the onset of a particular disease condition would also define a "real world" context of use in identifying potential candidates for preventive measures or further monitoring. On the other hand, the following are examples of situations that require or constitute carrying out further research to identify or reasonably confirm a "real world" context of use and, therefore, do not define "substantial utilities":

A. Basic research such as studying the properties of the claimed product itself or the mechanisms in which the material is involved.

B. A method of treating an unspecified disease or condition. (Note, this is in contrast to the general rule that treatments of specific diseases or conditions meet the criteria of 35 U.S.C. 101.)

C. A Method of assaying for or identifying a material that itself has no "specific and/or substantial utility".

D. A method of making a material that itself has no specific, substantial, and credible utility.

E. A claim to an intermediate product for use in making a final product that has no specific, substantial, and credible utility.

Note that "throw away" utilities do not meet the tests for a *specific* or *substantial* utility. For example, using transgenic mice as snake food is a utility that is neither specific (all mice could function as snake food) nor substantial (using a mouse costing tens of thousands of dollars to produce as snake food is not a "real world" context of use). Similarly, use of any protein as an animal food supplement or a shampoo ingredient are "throw away" utilities that would not pass muster as specific or substantial utilities under 35 U.S.C. 101. This analysis should, of course, be tempered by consideration of the context and nature of the invention. For example, if a transgenic mouse was generated with the specific provision of an enhanced nutrient profile, and disclosed for use as an animal food, then the test for specific and substantial *asserted* utility would be considered to be met.

"Well established utility" - a specific, substantial, and credible utility which is well known, immediately apparent, or implied by the specification's disclosure of the properties of a material, alone or taken with the knowledge of one skilled in the art. "Well established utility" does not encompass any "throw away" utility that one can dream up for an invention or a nonspecific utility that would apply to virtually every member of a general class of materials, such as proteins or DNA. If this is the case, any product or apparatus, including perpetual motion machines, would have a "well established utility" as landfill, an amusement device, a toy, or a paper weight; any carbon containing molecule would have a "well established utility" as a fuel since it can be burned; any protein would have well established utility as a protein supplement for animal food. This is not the intention of the statute.

See also the MPEP § 2107 - 2107.02.

Claims 1 and 3-7 remain rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility. The rejection is maintained for reasons of record as stated on pages 2-5 of the prior office action mailed 02/25/2003.

Applicants' arguments have been fully considered and are not persuasive. Applicant argues that SEQ ID NO:2 encodes a mouse homolog of the human CACNG8 gene as demonstrated by Exhibit B and that the CACNG8 gene was known at the time of filing. Applicant argues at the top of page 5 that the specification, at pages 3-4, clearly contemplates making an animal with a mutated form of the CACNG8 gene using the ES cells of claim 7. Applicant asserts that the animals clearly exhibit hyperactivity and have real world utility.

In response, Applicant's arguments implying the use of a mouse derived from the claimed ES cells apply only to the claims as they embody mouse ES cells as no other type of cell encompassed by the claims could be used to make an animal at the time of filing. The mouse derived from ES cells comprising an engineered mutation in a gene corresponding to SEQ ID NO:2 is not described in the specification of the instant invention and Applicant's assertions that the mouse clearly exhibits hyperactivity are unsupported. Without having the animal derived from ES cells comprising an engineered mutation in a gene corresponding to SEQ ID NO:2 of record, it cannot be assumed or predicted that the animals display a phenotype of hyperactivity or any other phenotype and thus, applicants' arguments do not support a use for the claimed ES cells in making the animal.

With respect to Applicant's assertion that Exhibit B is dispositive that SEQ ID NO:2 was known at the time of filing, it is noted that Exhibit B is a protein sequence, not a nucleic acid sequence, of a human CACNGLIKE3 gene. Exhibit B does not establish that SEQ ID NO:2 was known at the time of filing and Applicant has not explained, even if the gene was known at the time of filing, what the utility of the claimed cells would be. Applicant has not demonstrated what the well-established utility is supposed to be irrespective of whether the gene sequence or function was known at the time of filing. There is no evidence presented in Exhibit B demonstrating a functional role for the claimed gene. Without evidence that SEQ ID NO:2 actually encodes CACNG8, other than purported homology to a human gene, and without any data regarding a supported and established functional activity of SEQ ID NO:2, the utility of a knockout mouse or totipotent ES cell line, or any other cell comprising a disruption in SEQ ID

NO:2 is not readily apparent. The evidence of record at the time the claimed invention was filed, had not disclosed the identity or function of a gene comprising or encoding SEQ ID NO:2.

Further experimentation is required to determine what the direct or indirect effects of mutating the gene corresponding to SEQ ID NO: 2 will be on a murine cell, an ES cell or mouse made using the claimed ES cell. Thus, the evidence of record fails to support a well-established, specific or substantial utility of the claimed ES cells. Applicants have failed to point to a specific or substantial utility for the claimed invention and have failed to provide evidence of the asserted phenotype of a mouse made using the mouse ES cells encompassed by the claims. The claimed invention does not have a substantial utility because the specification does not show how to use the claimed cells without resorting to further research to determine the function of the gene whose expression is reduced in the claimed cell.

It is, therefore, maintained that the claimed mouse ES cell lines lack a specific and substantial utility until the gene is further characterized and identified as to its function. No genotype or phenotype of record is associated with SEQ ID NO:2. No gene function (or disruption thereof) is disclosed for any gene comprising the nucleotide sequence set forth in SEQ ID NO:2. The claimed product cannot be considered a research tool but rather is a material to be experimented upon.

Enablement

Claims 1 and 3-7 also remain rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. Specifically, since

the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

Written/Description/New matter

The rejection of claims 1 and 3-7 under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement is withdrawn in light of Applicant's amendments to the claims removing the objectionable claim language specific to the rejection set forth at pages 6-8 of the office action dated 02/25/2003. However, a new rejection based on Applicant's amendments to the claims is presented below.

Claims 1 and 3-7 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. 37 CFR 1.118 (a) states that "No amendment shall introduce new matter into the disclosure of an application after the filing date of the application".

Claims 1 and 7 have been amended to recite "the genetic locus encoding exon sequence presented in SEQ ID NO:2". As claimed, the gene is required only to comprise a part of SEQ ID NO:2 in an exon of said gene and that part can include any part, even a single nucleotide. Applicant points to the specification for support of these amendments at page 4, lines 29-32. However, page 4, lines 29-32 states only that the gene is that which is mutated by insertion of a

polynucleotide into a genetic locus that normally comprises polynucleotide sequence or post-spliced exonic sequence (interpreted to mean the DNA copy thereof) that is partially described in one of the GTS's of the sequence listing (i.e. SEQ ID NO:2). Thus, the specification only describes a gene encoding an mRNA that corresponds to the entire cDNA sequence of SEQ ID NO:2 and does not support the genus of genes encompassed by the claims wherein any gene comprising at least one exonic nucleotide in common with SEQ ID NO:2 is included in the genus.

MPEP 2163.06 notes, "If new matter is added to the claims, the examiner should reject the claims under 35 U.S.C. 112, first paragraph - written description requirement. In re Rasmussen, 650 F.2d 1212, 211 USPQ 323 (CCPA 1981)." MPEP 2163.02 teaches "Whenever the issue arises, the fundamental factual inquiry is whether a claim defines an invention that is clearly conveyed to those skilled in the art at the time the application was filed. If a claim is amended to include subject matter, limitations, or terminology not present in the application as filed, involving a departure from, addition to, or deletion from the disclosure of the application as filed, the examiner should conclude that the claimed subject matter is not described in that application. MPEP 2163.06 further notes "When an amendment is filed in reply to an objection or rejection based on 35 U.S.C. 112, first paragraph, a study of the entire application is often necessary to determine whether or not "new matter" is involved. Applicant should therefore specifically point out the support for any amendments made to the disclosure" (emphasis added).

Claim Rejections - 35 USC § 112-2nd paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 4-6 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 4 recites the limitation "genetically engineered mammalian cell" in line 1. There is insufficient antecedent basis for this limitation in the claim. Claim 1 has been amended to recite "genetically engineered murine cell" and thereby fails to provide antecedent basis for "genetically engineered mammalian cell". Claims 5 and 6 depend from claim 4.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 1 and 3-7 are rejected under 35 U.S.C. 102(a) and 35 U.S.C. 102(e) as being anticipated by Zambrowicz et al. (US 6,080,576, EFD 03/27/1998). The applied reference has a common inventor and assignee with the instant application. Based upon the earlier effective U.S. filing date of the reference, it constitutes prior art under 35 U.S.C. 102(e). This rejection under 35 U.S.C. 102(e) might be overcome either by a showing under 37 CFR 1.132 that any

invention disclosed but not claimed in the reference was derived from the inventor of this application and is thus not the invention "by another," or by an appropriate showing under 37 CFR 1.131.

Claims encompass a genetically engineered murine cell that is mutated by insertion of a polynucleotide into a genetic locus comprising any portion of SEQ ID NO:2. Claim 3 limits the cell to a mouse embryonic stem cell. Claim 4 limits the polynucleotide of claim 1 to one present on a viral vector. Claim 5 limits the viral vector to a retroviral vector. Claim 6 limits the viral vector to that additionally comprising targeting DNA that facilitate homologous recombination. Claim 7 is drawn to an isolated mouse ES cell line comprising a retroviral gene trap vector in a genetic locus comprising any portion of SEQ ID NO:2. The wording of the claims is such that they broadly encompass any genetic locus encoding any gene product as SEQ ID NO:2 includes all 4 nucleic acids, adenosine, guanine, cytosine and thymidine, at least one of which is necessarily present in all genes. The claims, as broadly written, merely require that some portion of the exonic sequence of SEQ ID NO:2, even a single nucleotide, be present in the locus that the polynucleotide inserts.

Zambrowicz ('576) taught a recombinantly manipulated retroviral gene trap vector that randomly inserts into the genome of a mouse (For example see col.1, lines 50-54; col. 3, lines 1-7; col. 28, lines 25-53). The vector is constructed in such a manner that when inserted into the genome of cells, only those cells comprising an insertion in a locus encoding a gene product (i.e. exons) are identified. '576 taught transfected mouse ES cells with the vector (col. 28, lines 55-63). The vector was capable of insertion into any gene and, therefore, the genetically engineered

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Valarie Bertoglio whose telephone number is (571) 272-0725. The examiner can normally be reached on Mon-Thurs 5:30-4:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla can be reached on (571) 272-0735. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Valarie Bertoglio
Examiner
Art Unit 1632